

## Letters to the Editor

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### Data analysis and interpretation of results in DATAS trial

Regarding the DATAS randomized study by Almendral *et al.*,<sup>1</sup> we would like to comment on methodological issues that may limit the validity of the results of this trial.

The investigators have created clinically significant adverse events (CSAEs) scoring system<sup>2</sup> based on assigning arbitrary weights to actual events that may artificially change the value of the analysed events, thus creating the potential of converting statistically insignificant result into a significant one. It is understandably difficult to model the outcome death, using such a CSAE scoring system and therefore the results could potentially underestimate the lethality of the interventions. Another source of modifying the observed difference between the two groups is the method of 'penalizing' for crossovers. Adding scores to both groups may not fully compensate for right censored data, but could artificially modify the difference between groups.

Furthermore, as paroxysmal atrial tachycardia was not an exclusion criterion, and dual-chamber (DC) implantable cardioverter defibrillators (ICDs) offered atrial anti-tachycardia functions, not surprisingly patients with single-chamber (SC) devices may experience a higher rate of long-duration atrial tachycardia. However, if some patients in the DC-ICD group received anti-tachycardia pacing or atrial shock, it is unclear whether this adverse event was not a reason for some crossovers. Given higher rates of both appropriate and inappropriate shocks in the DC-ICDs compared with SC-stimulated devices reported previously,<sup>3</sup> analysis of the causes of inappropriate shocks would be interesting.

Considering primary indications for ICD implantation, current registries show different rates of primary indications in different countries.<sup>4</sup> The DATAS sample population results may therefore have limited generalizability to other populations with conventional indications for ICD implantation.

Finally, as quality of life was to be evaluated as a secondary objective according to the study design,<sup>2</sup> it would be interesting to the readers to see these data published.

## References

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Zaruhi Vardanyan

Department of Medicine,  
Lincoln Medical and Mental Health Center,  
234 E 149 Street, Bronx, NY 10451, USA

Balavenkatesh Kanna

Weill Medical College of Cornell University,  
New York,  
NY, USA; and Department of Medicine,  
Lincoln Medical and Mental Health Center,  
234 E 149 Street, Bronx, NY 10451, USA  
Tel: +1 718 579 4842; fax: +1 718 579 4836.  
E-mail address: balavenkatesh.kanna@  
nychhc.org

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### Data analysis and interpretation of results in DATAS trial: reply

We appreciate the letter from Vardanyan and Kanna, which provides us with the opportunity to clarify some issues about the DATAS trial.

Studies comparing dual-chamber (DC) and single-chamber (SC) implantable cardioverter defibrillator (ICD) have so far focused on a single aspect of ICD therapy. Our aim was a global evaluation of their ability to reduce the clinically significant adverse events (CSAE) frequently suffered by ICD patients. Thus, we faced the challenge of evaluating patient outcome by a single variable. This would allow to (i) concentrate on alpha risk and (ii) have only one interpretation of the results as an answer to the objective question 'do DC-ICDs improve patient outcome by reducing CSAE?'

As patient evolution has to consider different undesired events, we decided to define a composite end-point, and that was mentioned in the DATAS design manuscript.<sup>1</sup> This strategy has two advantages: first, the possibility to concentrate patient evolution

in a single measure. This requires the assumption of clinical homogeneity,<sup>2</sup> i.e. that only aspects of similar medical relevance are pooled together and second, the chance to increase the study power allowing for smaller sample sizes. The required assumption is that of statistical homogeneity.<sup>3</sup>

The two 'softer' CSAE, i.e. inappropriate shocks and atrial tachyarrhythmias (AT), were 'hardened' in number and duration, respectively, to reinforce their clinical relevance. However, we believed that the assumption of clinical homogeneity was not met if death was pooled together with the other CSAE. We wanted to avoid, for example, that a patient with three hospitalizations had a worse score than a patient who died. The developed scoring system ensured that death, the worst expected outcome, had the highest score. Unplanned crossovers, a failure of the allocated treatment, received a relatively high score.

Although it has been demonstrated a higher rate of AT during follow-up in patients having them previously, this is presently neither a contraindication for ICD therapy nor an indication for DC-ICD. Thus, it was appropriate and justified to measure the potentially more active role of DC-ICD against AT. As described in the manuscript, inappropriate discharges were never a reason for premature crossover.

DATAS ICD indications, in accordance to contemporary guidelines, included secondary prevention in more than 85% of patients. Thus, the extent to which DATAS results could also apply to primary prevention patients is unclear.

We agree with Vardanyan and Kanna in the interest of the quality of life results, presently undergoing analysis.

## References

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Erik Cobo

Estadística e Investigacion Operativa  
Universitat Politècnica de Catalunya  
Barcelona  
Spain

**Aurelio Quesada**  
Cardiology Department  
Hospital General Universitario de Valencia  
Valencia  
Spain

**Fernando Arribas**  
Cardiology Department

*Hospital Universitario 12 de Octubre*  
Madrid  
Spain

**Jesús Almendral**  
Cardiology Department  
Hospital General Universitario Gregorio  
Marañón

5a Planta, 5100  
Dr Esquerdo 46  
Madrid  
Spain  
Tel: +34 91 586 8276  
Fax: +34 91 586 8018  
Email address: almendral@secardiologia.es